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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,953	10/15/2003	Kevin J. Rozeboom	066379-9001-02	7946

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/685,953	ROZEBOOM ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-46 and 50-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-46 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/13/2006
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 34-46 and 50-52 as amended (7/20/2006) are pending and under examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 34-37 as amended are rejected under 35 U.S.C. 102(b) as being anticipated by Naz et al. (IDS reference; Journal of Cellular Physiology. 1991, 146:156-163) in the light of evidence by US 5,864,021.

Claims are directed to a composition comprising 1) a reproductive cell and 2) a reproductive cell culture medium with at least one activated growth factor such as TGF beta 1 that is at least about 75% unbound growth factor. Some claims are further drawn to the use of the growth factor that is at least about 90% unbound growth factor.

The reference by Naz et al discloses a cell culture medium for sperm cells that comprises medium Ham's F-10 (page 157, col. 1, par. 2, line 6) and growth factor TGF beta or TGF beta-1 at concentration 5-50 ng/ml or 5000-50000 ng/L (see tables 1 and 2). TGF beta-1 is a purified preparation. It is known that chemical reagents or preparations of TGF are made in 95-99% purified form (unbound or not bound to contaminating or carrier proteins) as evidenced by US 5,864,021 (col. 9, lines 11-20 and col.11, lines 45-47). Thus, the growth factor in the cited medium composition is pure, unbound or activated growth factors within the meaning of the claims when read in the light of instant specification. Moreover, the cited reference by Naz et al.

teaches that the medium supplemented with growth factor has been found to be biologically functional as related to metabolic activity of sperm cells (page 158, col. 2, par. 2). Thus, the growth factor is reasonably expected to be in unbound form or in fully activated form within the meaning of the claims.

Therefore, the cited reference by Naz et al. anticipates the claimed invention.

2. Claims 34 and 44-46 as amended are rejected under 35 U.S.C. 102(b) as being by Lackey et al. (IDS reference; Archives or Andrology. 1998, 41:115-125) in the light of evidence by US 5,231,178.

Claims are directed to a composition comprising 1) a reproductive cell and 2) a reproductive cell culture medium with at least one activated growth factor such as insulin like growth factor (IGF-1) that is at least about 75% unbound growth factor. Some claims are further drawn to the use of the growth factor that is at least about 90% unbound growth factor.
The reference by Lackey et al discloses a cell culture medium for sperm cells that comprises a balanced salt buffer MTM or Tyrodes' medium and growth factor IGF-1 at concentration 100 ng/mL (abstract page 117). IGF is a purified preparation. It is known that chemical reagents or preparations of IGF are made in 95-99% purified form (unbound or not bound to contaminating or carrier proteins) as evidenced by US 5,231,178 (abstract). Thus, the growth factors in the cited medium composition are pure, unbound or activated growth factors within the meaning of the claims when read in the light of instant specification. Moreover, the cited medium supplemented with growth factor is found to be biologically functional as related to reproductive or sperm cells

(abstract, for example). Thus, the growth factor is reasonably expected to be in unbound form or in fully activated form within the meaning of the claims.

Therefore, the cited reference y Lackey et al. anticipates the claimed invention.

3. Claims 50-52 as amended are rejected under 35 U.S.C. 102(b) as being anticipated by Nocera et al. (IDS references; AJRI. 1995, 33:282-291) in the light of evidence by Lackey et al. (IDS reference; Archives or Andrology. 1998, 41:115-125).

Claims are directed to a composition comprising a sperm cell culture medium with 3 activated growth factors TGF beta 1, TGF beta 2 and IGF-1. Some claims are further drawn to the use of the activated growth factors that are at least about 75% unbound growth factor or at least about 90% unbound growth factor.

The reference by Nocera et al. teaches that seminal plasma contains growth factors in activated and latent from and that activation of latent forms is achieved by acid pH (abstract). In particular, the reference by Nocera et al. teaches presence of TGF beta 1 and TGF beta 2 in seminal plasma (abstract and table 1). The seminal plasma also contains IGF-1 as evidenced by Lackey et al. (page 116, par. 1-3). Thus, the acidified seminal plasma samples disclosed by Nocera et al. (for example: at page 284, col. 2, par. 3, lines 8-15) is a composition comprising all 3 factors TGF beta 1, TGF beta 2 and IGF-1 in activated form or 100% unbound. The acidified seminal plasma is a physiologically suitable medium for sperm cells and it also immunologically protect the integrity of sperm as taught by Nocera et al. (abstract, last lines).

Therefore, the cited reference by Nocera et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34-46 and 50-52 as amended are rejected under 35 U.S.C. 103(a) as being unpatentable over the reference by Naz et al. and the reference by Lackey et al. taken with reference by Nocera et al, US 5,864,021 and US 5,231,178.

Claims 34-46 are directed to a composition comprising 1) a reproductive cell and 2) a reproductive cell culture medium with at least one activated growth factor such as TGF beta 1 or TGF beta 2 or IGF-1 that is at least about 75% unbound growth factor. Some claims are further drawn to the use of the growth factor that is at least about 90% unbound growth factor.

Claims 50-52 are drawn to a medium composition intended for porcine sperm cells wherein the medium comprises all three growth factors TGF beta 1, TGF beta 2 and IGF-1 into the cell culture medium. Some claims are further drawn to the use of the growth factor that are at least about 75% or at least about 90% unbound growth factor.

The references by Naz et al. and by Lackey et al. are relied upon as explained above for the disclosure of animal sperm cell culture media with at least one purified or activated growth factor such as TGF beta or IGF-1. In particular, the reference by Naz et al. teaches incorporation of growth factor TGF beta 1 into sperm cell culture medium but it is silent with regard to growth factor IGF. However, the reference by Lackey et al teaches incorporation of IGF-1 into animal sperm cell culture medium. The reference by Lackey et al also teaches that growth factors

including IGF are present in animal seminal plasma and these factors provide for a natural environment for animal sperm cells. In addition, the reference by Nocera et al. teaches that other growth factors including TGF beta 1 and TGF beta 2 are also within animal seminal plasma and they activated in acidic environment.

The sperm cell medium compositions disclosed by Naz et al. and by Lackey et al. comprises the use of isolated and purified ingredients. It is known that chemical reagents including preparations of TGF and IGF are made in 95-99% purified form (unbound or not bound to contaminating or carrier proteins) as evidenced by US 5,864,021 (col. 9, lines 11-20 and col.11, lines 45-47) and by US 5,231,178 (abstract). Thus, the growth factors in the cited medium compositions are pure, unbound or activated growth factors within the meaning of the claims when read in the light of instant specification.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine growth factors including IGF-1, TGF beta 1 and TGF beta 2 in an animal sperm cell culture medium with a reasonable expectation of success in providing a physiologically suitable medium or environment for sperm cells because the physiologically suitable conditions provided by seminal plasma include growth factors that are presently claimed and because the prior art teaches incorporation of growth factors TGF beta and IGF into artificial cell culture media intended for sperm cells. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their

having been used individually in the prior art. In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Further, one of skill in the art would have been motivated to use activated, unbound or pure preparations of growth factors for the expected benefits in providing biologically functional culture medium environment. The concept of using "activated" or "unbound" factors is generic as claimed and when read in the light of specification.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34-46 and 50-52 as amended are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,849,394.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they both directed to substantially similar medium compositions comprising same components including reproductive or sperm cells and factors TGF beta 1, TGF beta 2 and IGF-1. The instant claims appear to be broader for being directed to a reproductive cell meaning a sperm cell. The instant claims appears to be narrower for reciting the term "unbound" factor that falls within the meaning of an isolated and purified biologically active reagent that would be normally used in biological applications and that are incorporated in composition(s) of the issued patent.

Accordingly, the claimed products in the issued patent and in the present application are obvious variants. Therefore, the inventions as claimed are co-extensive.

Response to Arguments

Applicant's arguments filed 7/20/2006 have been fully considered but they are not all found persuasive.

Claim rejection under 35 U.S.C. 102(b) as being anticipated by US 6,150,163 (McPerson et al) has been withdrawn because the medium disclosed by the cited patent does not contain a reproductive cell and/or because the medium disclosed by the cited patent does not contain all three factors in one medium as required by the presently amended claims.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by Naz et al. applicants argue that the cited medium does not contain TGF in activated and/or unbound form because the cited reference teaches that it discloses that TGF did not affect sperm function such as motility and egg penetration (response page 5). However, the idea that TGF did not affect sperm motility and egg penetration means that TGF did not have cytotoxic effects as the other factors tested in assays disclosed by Naz et al. The reference by Naz does not rule out that enzymatic induction in sperm cells by TGF have a role in sperm cell function (page 161, col. 2, par. 1). The medium disclosed by the cited reference contains isolated and purified reagent including TGF and, thus, they are "unbound" within the meaning of the claims, when read in the light of specification and as evidenced by US 5,864,021 as explained above.

With regard to the claim rejection under 35 U.S.C. 102(b) as being by Lackey et al. (IDS reference; Archives or Andrology. 1998, 41:115-125) applicants argue that the cited medium does not contain IGF in activated and/or unbound form because the cited reference teaches the use of IGF concentration higher than in the present invention (response page 6). Yet, the claimed invention is not so limited.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by Nocera et al. applicants argue that the cited medium is a seminal plasma not a "cell culture medium" as intended and explained by applicants' definitions (page 3, par. 000111) and as discussed in Declaration of Kevin Rozeboom submitted in the parent application (responses pages 7-8). Yet, the claimed invention is not limited by the same terms as defined by applicants and as argued before.

Claim rejection under 35 U.S.C. 103(a) as being unpatentable over US 6,150,163 (McPerson et al) has been withdrawn because the medium disclosed by the cited patent is not intended for porcine sperm cells as required by the presently amended claims.

With regard to the claim rejection under 35 U.S.C. 103(a) over the references by Naz et al., by Lackey et al. and by Nocera et al. applicants argue that there is no motivation and suggestion to combine references (response pages 12-14). However, motivation can come not only from direct teaching of the prior art, but also the nature of the problem to be solved and/or the knowledge of persons of ordinary skill in the art, Ruiz v. A.B. Chance Co. 357 F.3d 1270, 69 USPQ2d 1686 (2004). The cited references are in the same field of endeavor (such as compositions intended for storing and handling sperm cells) and they seek to solve the same problems as the instant application and claims (such as provide for a sperm cell medium), and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966). Further, the examiner recognizes that references cannot be arbitrarily combined that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references, *In re* Nomiya, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. One test for combining references is what the combination of disclosures taken as a whole would suggest to one versed in the art, rather than by their specific disclosures, *In re* Bozek, 163 USPQ 545 (CCPA 1969). In this case, the use of isolated and purified and, thus, "unbound" factors is known in the art, and the presently claimed factors have been used in

sperm cell medium for maintenance of sperm cell function. Thus, the combination of factors is considered to be obvious in the absence of evidence to the contrary.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (response page 13, par. 1) , it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

September 27, 2006

VERA AFREMOVA

PRIMARY EXAMINER